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Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference ZP0041	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP2003/004445	International filing date (day/month/year) 08 April 2003 (08.04.2003)	Priority date (day/month/year) 08 April 2002 (08.04.2002)
International Patent Classification (IPC) or national classification and IPC A61K 31/426, A61P 1/00, C07D 277/56		
Applicant ZERIA PHARMACEUTICAL CO., LTD.		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of _____ sheets.</p>	
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>	

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Date of submission of the demand 28 August 2003 (28.08.2003)	Date of completion of this report 13 January 2004 (13.01.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP2003/004445

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, as amended (together with any statement under Article 19  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
pages \_\_\_\_\_, as originally filed  
pages \_\_\_\_\_, filed with the demand  
pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

## 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP03/04445

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 9-12

because:

☒ the said international application, or the said claims Nos. 9-12 relate to the following subject matter which does not require an international preliminary examination (*specify*):

The inventions of claims 9-12 concern a method for treating the human body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 9-12

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP03/04445

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims		YES
	Claims	1-8	NO
Inventive step (IS)	Claims		YES
	Claims	1-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims		NO

## 2. Citations and explanations

- Document 1: EP 870765 A1 (ZERIA PHARMACEUTICAL CO., LTD.) October 14, 1998
- Document 2: JP 10-212271 A (ZERIA PHARMACEUTICAL CO., LTD.) August 11, 1998
- Document 3: EP 994108 A1 (ZERIA PHARMACEUTICAL CO., LTD.) April 19, 2000
- Document 4: WO 02/20010 A1 (ZERIA PHARMACEUTICAL CO., LTD.) March 14, 2002
- Document 5: MORITA, H., "Possible involvement of M5 muscarinic receptor in the enhancing actions of the novel gastroprokinetic agent Z-338 on nifedipine-sensitive voltage-dependent Ca<sup>2+</sup> currents in guinea pig stomach"  
Japanese Journal of Pharmacology (2002), Vol. 89, No. 4, pp. 356-365
- Document 6: KANEMOTO, Y., "An electrophysiological study of muscarinic and nicotinic receptors of rat paratracheal ganglion neurons and their inhibition by Z-338"  
British Journal of Pharmacology (2002), Vol. 135, No. 6, pp. 1403-1414
- Document 7: OGISHIMA, M., "Z-338 facilitates acetylcholine release from enteric neurons due to blockade of muscarinic autoreceptors in guinea pig stomach"  
Journal of Pharmacology and Experimental Therapeutics (2000), Vol. 294, No. 1, pp. 33-37
- Document 8: NAKAMIMA, T., "Z-338, a newly synthesized carboxamide derivative, stimulates gastric motility through enhancing the excitatory neurotransmission"  
Journal of Smooth Muscle Research (2000), Vol. 36, No. 2, pp. 69-81
- Document 9: FURUTA, S., "LC determination of Z-338, novel gastroprokinetic agent in dog plasma by SCX solid phase extraction"  
Journal of Pharmaceutical and Biomedical Analysis (2001), Vol. 25, No. 3-4, pp. 599-603

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

PCT/JP03/04445

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**Continuation of Box V:**

Based on the descriptions in documents 1-8 cited in the international search report, the inventions of claims 1-8 lack novelty and an inventive step.

Documents 1-9 state that 2-[N-(4,5-dimethoxy-2-hydroxy benzoyl) amino]-4-[(2-diisopropyl amino ethyl) amino carbonyl]-1,3-thiazole is useful for the prevention and treatment of generalized epigastric complaints, feelings of abdominal bloating, etc. (document 1, claims and page 10; document 2, claims and column 42; document 3, page 1; document 4, page 3; document 5, pages 356 to 365; document 6, pages 1403 to 1414; document 7, pages 33 to 37; document 8, pages 69 to 81; document 9, pages 599 to 603).

Gastric food competence is not specifically disclosed in documents 1-9, but the drugs used for the treatment of gastric food competence disorder in this application are also used for the prevention and treatment of feelings of early satiety and abdominal bloating, etc., and they are indistinguishable with respect to therapeutic use from drugs used for the treatment of generalized epigastric complaints and feelings of abdominal bloating, etc., which is the scope of application of existing drugs.

As a result, the inventions described in claims 1-8 are one and the same as the inventions described in documents 1-9.